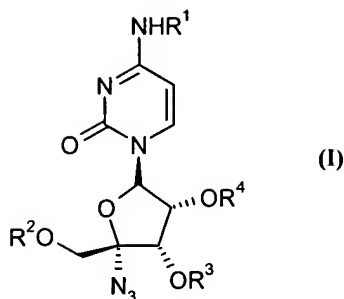


We claim:

1. A compound of formula I



wherein:

R¹ and R² are independently selected from the group consisting of hydrogen, COR⁵, C(=O)OR⁵, C(=O)SR⁵, C(=O)NHR⁵ and COCH(R⁶)NHR⁷;

R³ and R⁴ are independently selected from the group consisting of hydrogen COR⁵, C(=O)OR⁵, C(=O)SR⁵ and COCH(R⁶)NHR⁷; or, R³ and R⁴ taken together are selected from the group consisting of CH₂, C(CH₃)₂ and CHPh;

R⁵ is independently selected from the group consisting of C₁₋₁₈ unbranched or branched alkyl, C₁₋₁₈ unbranched or branched alkenyl, C₁₋₁₈ unbranched or branched alkynyl, C₁₋₁₈ lower haloalkyl, C₃₋₈ cycloalkyl, alkyl substituted C₃₋₈ cycloalkyl, phenyl optionally substituted with one to three substituents independently selected from the group consisting of halo, lower alkyl, lower alkoxy, lower thioalkyl, lower alkyl sulfinyl, lower alkyl sulfonyl, nitro, cyano, CH₂Ph wherein in phenyl ring is optionally substituted as described above, and CH₂OPh wherein in phenyl ring is optionally substituted as described above;

R⁶ is independently selected from the group consisting of the side chains of naturally occurring amino acids and C₁₋₅ unbranched or branched alkyl;

R⁷ is selected from the group consisting of hydrogen, R⁵OCO; or,

R⁶ and R⁷ taken together are (CH₂)₃; and,

hydrates, solvates, clathrates and acid addition salts thereof; with the proviso that at least one of R¹, R², R³, or R⁴ is other than hydrogen.

2. A compound according to claim 1 wherein R¹, R², R³, and R⁴ each are independently COR⁵, C(=O)OR⁵, C(=O)SR⁵ and each R⁵ is independently selected from the group consisting of C₁₋₁₈ unbranched or branched lower alkyl, phenyl and CH₂OPh.

3. A compound according to claim 2 wherein R^1 , R^2 , R^3 , and R^4 are COR^5 and each R^5 is independently selected from the group consisting of C_{1-18} unbranched or branched lower alkyl, phenyl and CH_2OPh .
- 5 4. A compound according to claim 1 wherein R^1 is COR^5 , $C(=O)OR^5$, $C(=O)SR^5$ or $COCH(R^6)NHR^7$ and R^2 , R^3 and R^4 are hydrogen.
- 10 5. A compound according to claim 4 wherein R^5 is selected from a group consisting of C_{1-18} unbranched or branched lower alkyl, C_{3-8} cycloalkyl, phenyl and CH_2OPh , or R^6 is selected from the group consisting of C_{1-5} unbranched or branched alkyl and the side chain of a naturally occurring amino acid.
- 15 6. A compound according to claim 1 wherein R^2 is selected from the group consisting of COR^5 , $C(=O)OR^5$, $C(=O)SR^5$, and $COCH(R^6)NHR^7$, R^1 , R^3 and R^4 are hydrogen.
- 20 7. A compound according to claim 6 wherein R^5 is selected from the group consisting of is C_{1-18} unbranched or branched alkyl, C_{3-8} cycloalkyl and phenyl or R^6 is C_{1-5} unbranched or branched alkyl or the side chain of a naturally occurring amino acid.
- 25 8. A compound according to claim 6 wherein R^2 is $COCH(R^6)NH_2$ and R^6 is selected from the group consisting of C_{1-5} unbranched or branched alkyl and CH_2Ph .
- 30 9. A compound according to claim 1 wherein R^3 and R^4 both are hydrogen.
10. A compound according to claim 1 wherein R^1 is hydrogen and R^2 , R^3 and R^4 are independently selected from the group consisting of COR^5 , $C(=O)OR^5$ and $C(=O)SR^5$.
11. A compound according to claim 1 wherein R^1 is hydrogen, R^2 is selected from the group consisting of COR^5 , $C(=O)OR^5$, $C(=O)SR^5$ and $COCH(R^6)NHR^7$, and R^3 and R^4 taken together are selected from the group consisting of CH_2 , $C(CH_3)_2$ and $CHPh$.
12. A compound according to claim 1 wherein R^1 and R^2 are hydrogen and R^3 and R^4 are independently selected from the group consisting of COR^5 , $C(=O)OR^5$, $C(=O)SR^5$ and $COCH(R^6)NHR^7$ wherein R^7 is hydrogen.

13. A compound according to claim 1 wherein R¹ and R² are independently selected from the group consisting of COR⁵, C(=O)OR⁵, C(=O)SR⁵ and COCH(R⁶)NHR⁷, and R³ and R⁴ taken together are selected from the group consisting of CH₂, C(CH₃)₂ and CHPh.

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14. A compound according to claim 1 selected from the group consisting of:

Isobutyric acid (2R,3S,4R,5R)-5-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-azido-4-isobutyryloxy-2-isobutyryloxymethyl-tetrahydro-furan-3-yl ester;

10 (S)-1-((3R,4S,5R)-5-Azido-3,4-bis-propionyloxy-5-propionyloxymethyl-tetrahydro-furan-2-yl)-2-oxo-1,2-dihydro-pyrimidin-4-yl-ammonium; chloride;

(S)-1-((3R,4S,5R)-5-Azido-3,4-bis-pentanoyloxy-5-pentanoyloxymethyl-tetrahydro-furan-2-yl)-2-oxo-1,2-dihydro-pyrimidin-4-yl-ammonium; chloride;

15

(S)-1-[(3R,4S,5R)-5-Azido-3,4-dihydroxy-5-(4-methyl-benzoyloxymethyl)-tetrahydro-furan-2-yl]-2-oxo-1,2-dihydro-pyrimidin-4-yl-ammonium; chloride;

20

(S)-1-((3R,4S,5R)-5-azido-3,4-bis-hexanoyloxy-5-hydroxymethyl-tetrahydro-furan-2-yl)-2-oxo-1,2-dihydro-pyrimidin-4-yl-ammonium; methanesulfonate;

(S)-1-((3R,4S,5R)-5-azido-5-hydroxymethyl-3,4-bis-pentanoyloxy-tetrahydro-furan-2-yl)-2-oxo-1,2-dihydro-pyrimidin-4-yl-ammonium; trifluoro-acetate;

25

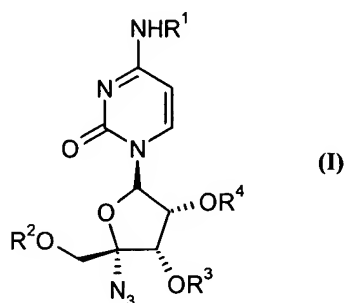
Tetradecanoic acid (2R,3S,4R)-5-((S)-4-amino-2-oxo-2H-pyrimidin-1-yl)-2-azido-3,4-dihydroxy-tetrahydro-furan-2-ylmethyl ester;

(S)-1-((3R,4S,5R)-5-azido-3,4-bis-butyryloxy-5-hydroxymethyl-tetrahydro-furan-2-yl)-2-oxo-1,2-dihydro-pyrimidin-4-yl-ammonium; trifluoro-acetate; and,

30

(S)-1-((3R,4S,5R)-5-Azido-5-decyloxy-carbonyloxymethyl-3,4-dihydroxy-tetrahydro-furan-2-yl)-2-oxo-1,2-dihydro-pyrimidin-4-yl-ammonium; trifluoro-acetate.

15. A method for treating diseases mediated by the Hepatitis C Virus (HCV) virus comprising administering to a mammal in need thereof, a therapeutically effective quantity of a compound of formula I



5 wherein:

R¹ and R² are independently selected from the group consisting of hydrogen, COR⁵, C(=O)OR⁵, C(=O)SR⁵, C(=O)NHR⁵ and COCH(R⁶)NHR⁷;

R³ and R⁴ are independently selected from the group consisting of hydrogen, COR⁵, C(=O)OR⁵, C(=O)SR⁵ and COCH(R⁶)NHR⁷; or, R³ and R⁴ taken together are selected from the group consisting of CH₂, C(CH₃)₂ and CHPh;

R⁵ is independently selected from the group consisting of C₁-₁₈ unbranched or branched alkyl, C₁-₁₈ unbranched or branched alkenyl, C₁-₁₈ unbranched or branched alkynyl, C₁-₁₈ lower haloalkyl, C₃-₈ cycloalkyl, alkyl substituted C₃-₈ cycloalkyl, phenyl optionally substituted with one to three substituents independently selected from the group consisting of halo, lower alkyl, lower alkoxy, lower thioalkyl, lower alkyl sulfinyl, lower alkyl sulfonyl, nitro, cyano, CH₂Ph wherein in phenyl ring is optionally substituted as described above, and CH₂OPh wherein in phenyl ring is optionally substituted as described above;

R⁶ is independently selected from the group consisting of the side chains of naturally occurring amino acids and C₁-₅ unbranched or branched alkyl;

R⁷ is selected from the group consisting of hydrogen, R⁵OCO; or,

R⁶ and R⁷ taken together are (CH₂)₃; and,

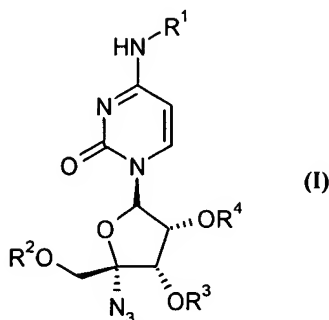
hydrates, solvates, clathrates and acid addition salts thereof; with the proviso that at least one of R¹, R², R³, or R⁴ is other than hydrogen.

- 25 16. The method of claim 15 wherein R¹, R², R³, and R⁴ are each independently COR⁵, C(=O)OR⁵, C(=O)SR⁵ and R⁵ is independently selected from the group consisting of C₁-₁₈ unbranched or branched lower alkyl, C₃-₈ cycloalkyl, phenyl and CH₂OPh.

17. The method of claim 16 wherein R^1 , R^2 , R^3 , and R^4 are each independently COR^5 and R^5 is independently selected from the group consisting of C_{1-18} unbranched or branched lower alkyl, C_{3-8} cycloalkyl, phenyl and CH_2OPh .
- 5 18. The method of claim 15 wherein R^1 is COR^5 , $C(=O)OR^5$, $C(=O)SR^5$ or $COCH(R^6)NHR^7$ and R^2 , R^3 and R^4 are hydrogen.
- 10 19. The method of claim 18 wherein R^5 is selected from a group consisting of C_{1-18} unbranched or branched lower alkyl, C_{3-8} cycloalkyl, phenyl and CH_2OPh , or R^6 is selected from the group consisting of C_{1-5} unbranched or branched alkyl and the side chain of a naturally occurring amino acid and R^7 is hydrogen.
- 15 20. The method of claim 15 wherein R^2 is selected from the group consisting of COR^5 , $C(=O)OR^5$, $C(=O)SR^5$, and $COCH(R^6)NHR^7$, R^1 , R^3 and R^4 are hydrogen.
- 20 21. The method of claim 20 wherein R^5 is selected from the group consisting of is C_{1-18} unbranched or branched alkyl, C_{3-8} cycloalkyl or phenyl or, R^6 is C_{1-5} unbranched or branched alkyl or the side chain of a naturally occurring amino acid.
22. The method according to claim 20 wherein R^2 is $COCH(R^6)NH_2$ and R^6 is selected from the group consisting of C_{1-5} unbranched or branched alkyl or CH_2Ph .
23. The method of claim 15 wherein R^3 and R^4 both are hydrogen.
- 25 24. The method of claim 15 wherein R^1 is hydrogen and R^2 , R^3 and R^4 are independently selected from the group consisting of COR^5 , $C(=O)OR^5$, $C(=O)SR^5$.
25. The method of claim 15 wherein R^1 is hydrogen, R^2 is selected from the group consisting of COR^5 , $C(=O)OR^5$, $C(=O)SR^5$ and $COCH(R^6)NHR^7$, and R^3 and R^4 taken together are selected from the group consisting of CH_2 , $C(CH_3)_2$ and $CHPh$.
- 30 26. The method of claim 15 wherein R^1 and R^2 are hydrogen and R^3 and R^4 are independently selected from the group consisting of COR^5 , $C(=O)OR^5$, $C(=O)SR^5$ and $COCH(R^6)NHR^7$ wherein R^7 is hydrogen.

- 5
27. The method of claim 15 wherein R^1 and R^2 are selected from the group consisting of COR^5 , $C(=O)OR^5$, $C(=O)SR^5$ and $COCH(R^6)NHR^7$, and R^3 and R^4 taken together are selected from the group consisting of CH_2 , $C(CH_3)_2$ and $CHPh$.
28. The method of Claim 15 wherein the compound is delivered in a dose of between 1 and 100 mg/kg of body weight of the patient per day.
29. The method of claim 15 wherein the mammal is a human.
- 10
30. The method of Claim 15 further comprising administering at least one immune system modulator and/or at least one antiviral agent that inhibits replication of HCV.
31. The method of Claim 30 further comprising administering an immune system modulator.
- 15
32. The method of Claim 31 wherein the immune system modulator is an interferon, interleukin, tumor necrosis factor or colony stimulating factor or an anti-inflammatory agent.
33. The method of Claim 32 wherein the immune system modulator is an interferon or chemically
- 20
- derivatized interferon.
34. The method of claim 33 wherein the immune system modulator is interferon- α or chemically derivatized interferon- α .
- 25
35. The method of Claim 30 further comprising administering at least one other antiviral agent.
36. The method of claim 35 where the antiviral compound is selected from the group consisting of an HCV protease inhibitor, another HCV polymerase inhibitor, an HCV helicase inhibitor, an HCV primase inhibitor and an HCV fusion inhibitor.
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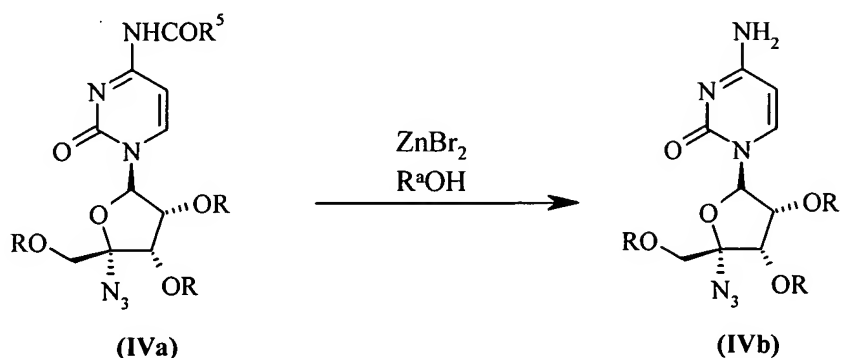
37. A pharmaceutical composition comprising a therapeutically effective quantity of a compound of formula I



wherein:

- 5 R^1 and R^2 are independently selected from the group consisting of hydrogen, COR^5 , $C(=O)OR^5$, $C(=O)SR^5$, $C(=O)NHR^5$ and $COCH(R^6)NHR^7$;
- R^3 and R^4 are independently selected from the group consisting of hydrogen, COR^5 , $C(=O)OR^5$, $C(=O)SR^5$ and $COCH(R^6)NHR^7$; or, R^3 and R^4 taken together are selected from the group consisting of CH_2 , $C(CH_3)_2$ and $CHPh$;
- 10 R^5 is independently selected from the group consisting of C_{1-18} unbranched or branched alkyl, C_{1-18} unbranched or branched alkenyl, C_{1-18} unbranched or branched alkynyl, C_{1-18} lower haloalkyl, C_{3-8} cycloalkyl, alkyl substituted C_{3-8} cycloalkyl, phenyl optionally substituted with one to three substituents independently selected from the group consisting of halo, lower alkyl, lower alkoxy, lower thioalkyl, lower alkyl sulfinyl, lower alkyl sulfonyl, nitro, cyano, CH_2Ph
- 15 wherein in phenyl ring is optionally substituted as described above, and CH_2OPh wherein in phenyl ring is optionally substituted as described above;
- R^6 is independently selected from the group consisting of the side chains of naturally occurring amino acids and C_{1-5} unbranched or branched alkyl;
- R^7 is selected from the group consisting of hydrogen, R^5OCO ; or,
- 20 R^6 and R^7 taken together are $(CH_2)_3$; and,
- hydrates, solvates, clathrates and acid addition salts thereof; in combination with one or more pharmaceutically acceptable carriers and excipients, with the proviso that at least one of R^1 , R^2 , R^3 , or R^4 is other than hydrogen.

38. A process for converting an N-acyl cytidine compound **IVa** to a cytidine compound **IVb** by selective cleavage of an N-acyl moiety from **IVa** wherein:



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R is independently selected from the group consisting of hydrogen, COR⁵, C(=O)OR⁵, C(=O)SR⁵, C(=O)NHR⁵ and COCH(R⁶)NHR⁷;

R⁵ is independently selected from the group consisting of C₁₋₁₈ unbranched or branched alkyl, C₁₋₁₈ unbranched or branched alkenyl, C₁₋₁₈ unbranched or branched alkynyl, C₁₋₁₈ lower haloalkyl, C₃₋₈ cycloalkyl, alkyl substituted C₃₋₈ cycloalkyl, phenyl optionally substituted with one to three substituents independently selected from the group consisting of halo, lower alkyl, lower alkoxy, lower thioalkyl, lower alkyl sulfinyl, lower alkyl sulfonyl, nitro, cyano, CH₂Ph wherein in phenyl ring is optionally substituted as described above, and CH₂OPh wherein in phenyl ring is optionally substituted as described above;

R⁶ is independently selected from the group consisting of the side chains of naturally occurring amino acids and C₁₋₅ unbranched or branched alkyl;

R⁷ is selected from the group consisting of hydrogen, R⁵OCO; or,

R⁶ and R⁷ together are (CH₂)₃;

said process comprising contacting a solution of said N-acyl pyrimidine nucleoside with ZnBr₂ in a protic solvent R^bOH wherein R^a is hydrogen or C₁₋₄ alkyl.

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